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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/727,769	12/04/2000	Shotaro Yamaguchi	Q62106	5479

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Sughrue Mion Zinn Macpeak & Seas PLLC
2100 Pennsylvania Avenue NW
Washington, DC 20037-3213

EXAMINER

RAO, MANJUNATH N

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 08/13/2002

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n No.

09/727,769

Applicant(s)

YAMAGUCHI, SHOTARO

Examiner

Manjunath N Rao

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 June 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) 1-20, 22 and 23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21, 24 and 25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>8</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Claims 1-25 are still at issue and are present for examination. Claims 21, 24-25 are now under consideration. Claims 1-20, 22-23 have been withdrawn from consideration as being drawn to non-elected invention.

Election/Restrictions

Applicant's election without traverse of Group III, claims 21, 24-25 in Paper No. 13 is acknowledged.

Priority

It is noted that this application appears to claim subject matter disclosed in prior copending Application No. 09/324,910, filed 6-3-1999. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). Also, the current status of all nonprovisional parent applications referenced should be included.

If the application is a utility or plant application filed on or after November 29, 2000, any claim for priority must be made during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2) and (a)(5). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim

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for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) a surcharge under 37 CFR 1.17(t), and (2) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Commissioner may require additional information where there is a question whether the delay was unintentional. The petition should be directed to the Office of Petitions, Box DAC, Assistant Commissioner for Patents, Washington, DC 20231.

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The priority document is in Japanese and as the Examiner does not read or understand Japanese, an English translation of the priority document is required for perfecting the priority.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21 and 24-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All three above claims recite the phrase “and cross-linking of protein to react with a/the protein and/or a peptide/food”. It is unclear to the Examiner as to which “protein” applicant is referring to in the above phrase, whether it the protein that is being acted upon by the enzyme or cross-linking of another protein to the protein that is being acted

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upon. It is also not clear to the Examiner as to which protein applicants are referring to recited in the second part of the phrase.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21, 24-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of deamidating amido groups in protein or peptides in a food using the deamidating enzyme with SEQ ID NO:6, does not reasonably provide enablement for such a method using any deamidating enzyme from any source. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 21, 24-25 are specifically drawn to a method of deamidating proteins using an enzyme, which directly acts upon the groups without causing severing of peptide bond and cross-linking of that protein with another protein or a peptide, and which appears to be a unique property of the enzyme with SEQ ID NO:6. However, claims 21, 24-25 are so broad as to

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encompass a method of deamidating proteins using any deamidase from any source and applicants have not taught as to how one of skill in the art would be able make or find such an enzyme. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of sources broadly encompassed by the claims. Furthermore, even if one of ordinary skill in the art contemplates on making such an enzyme by recombinant methods by mutating known deamidases, the specification does not provide enablement. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence to obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only one such amidase.

While enzyme isolation and characterization methods are known in the art, it is not routine in the art to screen exhaustively large number of sources to find the desired enzyme and such screening would also cause undue experimentation to one of ordinary skill in the art. Similarly, while recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications of known deamidases, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In

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addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all sources of the enzyme and all modifications and fragments of any amidase because the specification does not establish: (A) a rational and predictable scheme for isolating the enzyme from any or all given sources; (B) a rational and predictable scheme for modifying any known amidase amino acid residue with an expectation of obtaining the desired biological function; (C) regions of the protein (any amidase) structure which may be modified; (D) the general tolerance of deamidases to modification and extent of such tolerance; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including deamidases isolated from any source. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, identification and determination of amidase having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 21, 24-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

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skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 21, 24-25 are directed to a method of deamidating proteins using enzymes from any source. Claims 21, 24-25 are rejected under this section of 35 USC 112 because the claims are directed to a method which uses a genus of polypeptides (derived from any source including recombinantly modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution) that have not been disclosed in the specification. No description has been provided of the modified polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:6 has been provided by applicants which would indicate that they had possession of the claimed genus of polypeptides. The specification does not contain any disclosure of the structure of all the polypeptides including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structures. Therefore many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 21 is rejected under 35 U.S.C. 102(a) as being anticipated by Yamaguchi et al. (Appl. Environ. Microbiol., 8/2000, Vol. 66(8):3337-3343). This rejection is based upon the public availability of a printed publication published by others. Claim 21 of the instant application is drawn to a method of modifying a protein or a peptide by allowing an enzyme -- having an activity to deamidate amido groups in protein or peptide—to directly act upon the amido groups without causing severing of the peptide bond and cross-linking of the protein to another protein or peptide. Yamaguchi et al. disclose such a method using such an enzyme (see entire document especially page 3337, under Materials and Methods, last para). Thus Yamaguchi et al. anticipate claim 21 of this application as written.

Claims 21, 24-25 are rejected under 35 U.S.C. 102(a) as being anticipated by Yamaguchi et al. (EP 0976829 A2, 2-2-2000). This rejection is based upon the public availability of a printed publication published by others. Claims 21, 24-25 of the instant application is drawn to a method of modifying a protein or a peptide by allowing an enzyme -- having an activity to deamidate amido groups in protein or peptide by directly acting upon the amido groups without causing severing of the peptide bond and cross-linking of the protein to another protein or peptide—to act on specific peptides, proteins (either of animal or plant origin) or foods comprising such proteins. Yamaguchi et al. disclose identical method for deamidating a peptide or a protein using an identical enzyme (see entire document, specifically see claims 19, 21-22). Thus Yamaguchi et al. anticipate claims 21, 24-25 of this application as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamaguchi et al. as applied to claim 21 above, and further in view of Hamada et al. (J. Food Sci., 1989, Vol. 54(3):598-602. Claims 24-25 in this instant application are drawn to a method for improving functionality of a plant or animal protein and/or peptide based food by allowing an enzyme -- having an activity to deamidate amido groups in proteins or peptides by directly act upon the amido groups without causing severing of the peptide bond and cross-linking of the protein to another protein or peptide—to act on such proteins or foods comprising such proteins.

Yamaguchi et al. as it applies to claim 21 has already been explained above. While Yamaguchi et al. teach the enzyme and its use to deamidate a short peptide, the reference does not teach the use of the enzyme to improve functionality of plant or animal proteins or foods containing such proteins.

Hamada et al. teach that functional properties of food proteins such as soy proteins (plant protein) or casein (animal protein) depends on their conformation and that the conversion of protein amide groups to carboxyl groups by deamidation improves properties such as solubility and other physical characteristics. The reference also teaches that such improved properties enhance their use as functional ingredients in food systems such as beverages, dressings, toppings and confections et c. Hamada et al. in fact, teach the use of a deamidase isolated from

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B.circulans. However, the reference also makes it clear that the enzyme from *B.circulans* its activity towards intact protein is small and that the enzyme prefers peptides. The reference also teaches that use of the *B.circulans* also results in bitter peptides as it hydrolyzes the peptide bond and releases bitter peptides.

Using the reference of Yamaguchi et al. and that of Hamada et al. it would be obvious to one of ordinary skill in the art to use the enzyme of Yamaguchi et al. for deamidating large or intact proteins especially those used in the food industry. One of ordinary skill in the art would have been motivated to do so because Yamaguchi et al. teach an enzyme which directly acts on the amido groups without acting on the peptide bond and Hamada et al. teach that the known enzymes in the art used for improving the functionality of the food proteins such as that from *B.circulans* prefers only small peptides and is not efficient on large or intact proteins and also releases bitter peptides into the food. One of ordinary skill in the art would have a reasonable expectation of success as Yamaguchi et al. teach the enzyme with unique properties described above and Hamada et al. teach the importance of improving the functionality food proteins and also the disadvantages of using the presently known deamidases.

Therefore the above invention would have been *prima facie* obvious to one of ordinary skill in the art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

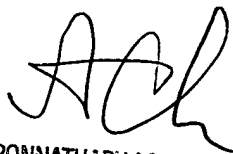
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the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath Rao whose telephone number is (703) 306-5681. The Examiner can normally be reached on M-F from 8:00 a.m. to 4:30 p.m. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, P.Achutamurthy, can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Manjunath N. Rao
August 12, 2002